

# A Computer Operated Mass Spectrometer System

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**An integer resolution mass spectrometer-computer system has been developed in which the computer controls the "scan" of a mass spectrometer. In this system, the computer queries the user for operating parameters which are then translated into control functions which operate the mass analyzer. The spectral information acquired from the mass spectrometer is made available to the chemist within minutes in an on-line graphic system. Examples of the processing of GLC effluent are given.**

THE USE OF MASS SPECTROMETRY has been hampered by the lagging development of a fast and convenient method of reducing the spectral output of the mass spectrometer (MS) to numerical data. Usually the operator must convert a MS chart recording, which is an analog plot of intensity *vs.* time, to a digitized plot of intensity *vs.* mass number. Because of instrument instabilities, wide range of signal amplitudes, large amounts of data, and other operational difficulties, (1, 2), it is often difficult and time-consuming to establish all the correct mass peak identifications. One aid is to use a reference compound (3) either prior to the run or as an internal standard with the unknown sample. By counting from known mass peaks, unknown spectral peaks can be identified. However, the processing of data by this technique is still a formidable task and it may take several days to accumulate all the information from a gas chromatograph-mass spectrometer (GLC-MS) run.

Several workers have demonstrated MS-computer systems in which the computer monitors and records digital data from a MS. In most of these applications the mass spectrometer has operated independently of the computer, scanning in some time dependent mode, measuring ion intensities at all points within the range of (500 to 5000 samples per second) and afterward performs the computations required to reduce the large amounts of digital data to useful information (4-7). Much instrument time and sampling effort is expended in the intervals between integer peak positions where there is little or no information. One system that improved

upon this latter inefficiency used step switches to step the scan from position to position (8).

We now describe a MS-computer system, suitable for routine laboratory use, in which the computer controls the operation of a quadrupole mass spectrometer (9, 10). In this system the "scan" is calibrated by relating known mass positions of a reference compound to a computer generated control voltage ( $V_c$ ).  $R_c$  is generated as the result of a number  $N$ , sent from the computer to a Digital-to-Analog (D-to-A) converter in a MS-computer interface. The parameters of this  $V_c$ , or the  $N$  for each integer mass position, are determined by a computer program and stored in memory. The subsequent use of this information allows the computer-directed MS output to be recorded directly as mass/charge ( $m/e$ ) *vs.* intensity. On request, this data is then made available to the operator in an on-line system.

The use of this computer-MS interaction, combined with the decision-making ability of the operator, permits a significant saving in data processing costs. Furthermore, a much larger duty cycle of analyzer "on peak" time is obtainable, resulting in the detection of more ions for a given mass position than is possible in conventional time based scanning.

The new MS-computer system has at least three unique features. There is a hardware control interface to connect the MS intimately with the computer; there is an improved efficiency of information acquisition from spectral peaks that are limited in ion production rates; and there is a user-oriented control and data presentation system that conceals the foregoing details from the operator, but presents the user with prompt and concise data which include normalized mass spectral plots.

The described system has evolved through three mass spectrometers, three computers, and two basic computer programs (11, 12). The later systems have greater range, sensitivity, and convenience, but they all have a common concept. Therefore the description that follows will be conceptual rather than specific to any one configuration.

- (1) K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, 1962, p 10.
- (2) J. Lederberg, E. Levinthal, and Staff, "Cytochemical Studies of Planetary Microorganisms Explorations in Exobiology," IRL Report No. 1054, Instrumentation Research Laboratory, Department of Genetics, Stanford University School of Medicine, April 1966 to October 1966. NASA Accession No. N66-34795.
- (3) J. H. Beynon, "Mass Spectrometry and Its Applications to Organic Chemistry," Elsevier Publishers, Amsterdam, 1960, p 44.
- (4) R. A. Hites and K. Biemann, *ANAL. CHEM.*, **39**, 965 (1967).
- (5) *Ibid.*, **40**, 1217 (1968).
- (6) R. A. Hites, S. Markey, R. C. Murphy, and K. Biemann, 16th *Ann. Conf. Mass Spectrometry Allied Topics*, ASTM E-14, Pittsburgh, Pa., May 1968.
- (7) R. B. Tucker, "A Mass Spectrometer Data Acquisition and Analysis System," IRL Report No. 1063, Instrumentation Research Laboratory, Department of Genetics, Stanford University School of Medicine, NASA Accession No. N68-25743, 1968.

- (8) H. L. Friedman, H. W. Goldstein, and G. A. Griffith, "Mass Spectrometric Thermal Analysis of Polymer Decomposition Products," 15th *Ann. Conf. Mass Spectrometry Allied Topics*, ASTM E-14, Denver, Colo., May 1967.
- (9) W. E. Reynolds, "A Small Computer Approach to Low Resolution Mass Spectrometry," Pacific Conference on Chemistry and Spectroscopy, Anaheim, Calif., November 1967.
- (10) W. E. Reynolds, T. B. Coburn, J. Bridges, and R. Tucker, "A Computer Operated Mass Spectrometer System," IRL Report No. 1062, Instrumentation Research Laboratory Department of Genetics, Stanford University School of Medicine, NASA Accession No. N68-11869, Nov. 1967.
- (11) W. E. Reynolds, R. B. Tucker, R. A. Stillman, and J. C. Bridges, "Mass Spectrometers in a Time Shared Computer Environment," 17th *Ann. Conf. Mass Spectrometry Allied Topics*, ASTM E-14, 1969.
- (12) J. Lederberg, E. Levinthal, and Staff, "Cytochemical Studies of Planetary Microorganisms Explorations in Exobiology," IRL Report No. 1076, Instrumentation Research Laboratory, Department of Genetics, Stanford University School of Medicine, October 1967 to April 1968. Appendix A is a published reprint of the above "Mass Spectrometers in a Time Shared Environment," NASA Accession No. N68-29546.

## INSTRUMENTATION

The present system is operating with a Finnigan 1015 quadrupole MS and a Varian Aerograph 600D chromatograph. The same computer programs and a similar interface were also operated successfully with a Bendix Time-of-Flight (T-o-F) MS (13) and an EAI quadrupole (14) MS. In all cases the GLC-MS, the teletypewriter, and the digital plotter were situated in a wet chemical laboratory.

A schematic diagram of the GLC-MS combination is shown in Figure 1. The effluent from the gas chromatograph, equipped with a flame ionization detector, first passes through a variable splitter that diverts between  $\frac{1}{3}$  and  $\frac{1}{2}$  of the flow through a Biemann separator (15) and into the MS. A solenoid-actuated valve in this line helps to keep the large initial solvent peak from entering the MS system. A reference gas reservoir containing a fluorine compound at a vapor pressure of approximately  $3 \times 10^{-7}$  Torr is also incorporated in the system and is connected to the MS by another solenoid valve. The computer, via the interfacing electronics, has direct control of gas valves, and can valve in or shut off the reference gas whenever it is needed for the calibration routine.

These valves were constructed in our shops in such a way that the back side is open to the vacuum system when the valve is closed. This avoids the common pressure burst when conventional valves are opened to a vacuum.

The right side of Figure 1 illustrates the major components and functions of the interface. This computer-MS interface was built in our Instrumentation Research Laboratory (16) and contains all the electronics not normally supplied with a standard configuration MS or computer. All of the operating parameters of the MS are, or may be, controlled by a digital word (binary number) sent from the computer. The principal control is via the "N" register to the D-to-A converter. The analog signal,  $V_c$ , from the D-to-A sets and holds the mass analyzer to pass ions of a predetermined  $m/e$ . Alternately the digital output may be coded to operate auxiliary control functions, such as actuate valves, set amplifier gains, the low speed multiplexer, or enable the digital plotter.

The characteristic method of controlling the  $m/e$  passband and taking measurements while the mass analyzer dwells upon a  $m/e$  value converts what is normally measured as a time dependent parameter, to a stationary signal. This statistically stationary property of the signal enables the employment of full integration to enhance signal to noise. Both the electrometer and the integrator are standard commercial FET operational amplifiers of the \$50.00 class. The time allowed for integration and the operation of the integrator reset are controlled by signals (numbers) from the computer to the "T" register. The output of the integrator is sampled, held, and read via the Analog-to-Digital (A-to-D) converter.

Auxiliary signal sensing is provided by the low speed multiplexer. This is useful to determine the automatic settings for self calibration, or may be used to record temperature, pressure, etc. These sense functions, plus some valve

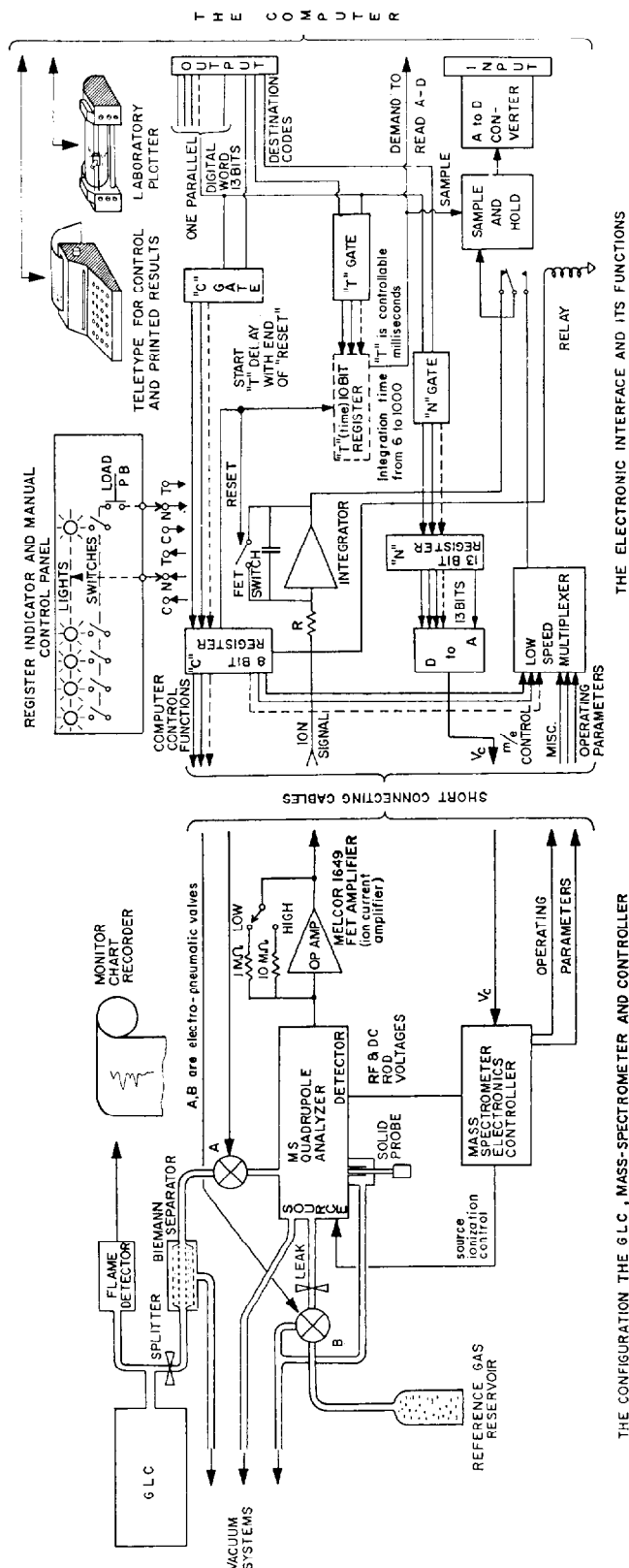


Figure 1. The GLC-MS instrumentation and the electronics interface to enable computer systems integration

control and checkout functions, are controlled by the "C" register.

There are no manual operator control functions in any of the above steps. The control is accomplished at the teletypewriter keyboard. This keeps the system flexible and makes it independent of the idiosyncrasies of individual computer

- (13) D. B. Harrington and R. S. Gohlke, "High Resolution Time of Flight Mass Spectrometers," 10th Ann. Conf. Mass Spectrometry Allied Topics, ASTM E-14, New Orleans, La., 1962.
- (14) W. Paul, H. P. Reinhard, and U. von Zahn, *Z. Phys.*, **152**, 143 (1958).
- (15) J. T. Watson and K. Biemann, *ANAL. CHEM.*, **37**, 844 (1965).
- (16) W. E. Reynolds, J. C. Bridges, R. B. Tucker, and T. B. Coburn, "Computer Control of Mass Analyzers," 16th Ann. Conf. Mass Spectrometry Allied Topics, ASTM E-14, Pittsburgh, Pa., 1968.

COMPUTER DIALOGUE  
(The user's response is underlined)

OPTION = collect  
EXPERIMENT# = test  
  
T = 35  
  
MODE = single  
  
PLOT, TYPE, or FILE = plot  
  
BY MASS, AMP, or ENTIRE = entire  
  
FROM MASS = 1  
TO = 510  
QUICK = n  
  
  
PLOT, TYPE, or FILE = /  
T = /  
EXPERIMENT# = MS26x15  
CONTINUATION = yes  
T = 6  
MODE = continuous  
  
# OF SPECTRA = 130  
FILED IN POSITIONS 940 to 1070  
T = /  
EXPERIMENT# = /  
OPTION = sum  
EXP# = MS26x15  
FROM SPECTRUM = 940  
TO = 1020  
FROM MASS = 40  
  
TO MASS = 500  
PLOT = yes  
  
  
EXP# = /  
OPTION = plot  
EXPERIMENT# = MS26x15  
FROM SPECTRUM = 957  
TO = 957  
FROM MASS = 1  
TO MASS = 340

COMMENT

The user requests the data collection phase.  
A catch-all name, "test", is given; the spectrum will be used simply for a systems check.  
An integration time of 35 milliseconds per peak is requested.  
Only one spectrum will be taken (single mode).  
The data is acquired after this answer.  
The user can plot, type, or file the data collected; here a plot is requested.  
The user can plot selected masses, the highest intensities, or the entire spectrum within requested limits.  
The user indicates the limits.  
  
A QUICK plot omits annotation, etc.  
Note that "y" and "n" mean "yes" and "no".  
The user completed the checkout and now wishes to proceed with the experiment.  
The "/" is used to backup through the conversation.  
An existing experiment name is given here.  
The user confirms that the spectra are to be added to the existing experiment file.  
The user requests that spectra be collected continuously until 130 are taken.  
  
Data collection is complete.  
  
The user then wishes to sum the elements of each spectrum to produce a "total ion" plot, analogous to a GLC trace.  
  
Mass position 40 to 500 are summed for each of the collected spectra.  
  
The "total ion" curve is now plotted.  
(Figures 6 and 7 are illustrative of this sample dialogue.)  
Guided by the total ion plot, the user will plot interesting mass spectra.  
Only the spectrum filed in position 957 is chosen.  
  
The plot (Figure 17) is drawn and normalized to the base peak,  $m/e = 31$ .

Figure 2. An example of the user-computer dialogue during operation

interrupt lines and/or individual computer characteristics. This straightforward system definition makes the software design much like conventional computer programming rather than encouraging intricate techniques highly dependent upon the specific hardware.

Thus the system is not oriented specifically to any given computer. It has operated on an early model LINC (17) computer with 2K words of 12 bits, memory, and on a time-shared, locally programmed, IBM 360/50, buffered with an IBM 1800 (18). In all cases the computer was somewhat remote, separated by some 500 ft of cable from the rest of the instrumentation. The system is very economical of computer resources. Most of today's small general purpose computers would be able to operate the described functions if it were desired to avoid time-shared computer dependency. Some

sort of magnetic storage for object code programs and data storage is most desirable. DEC-type tapes have been used on the LINC system and disc packs on the IBM system.

THE SOFTWARE STRUCTURE

The objectives of the software are to operate and control the MS, acquire data from the MS, process and present this data in a manner useful to the chemist, and provide certain control and information to aid in maintaining and servicing the instrument.

With the program loaded into the computer, the user requests any one of several functions (see Table I) by typing the name of that function. The computer responds with a series of prompts (see Figure 2) to elicit user macrocommands. The computer then generates the detailed control functions to perform the assigned task. At the completion of the task, requests are made for new parameters. By striking the slash ("/"), the user can "backup" through any conversation to correct errors or to go to a different function. This conversation technique makes the system both flexible and reasonably self-instructing.

(17) R. W. Stacy and B. Waxman, "Computers in Biomedical Research," Vol. II, Academic Press, New York, N. Y., 1965, pp 35-66.

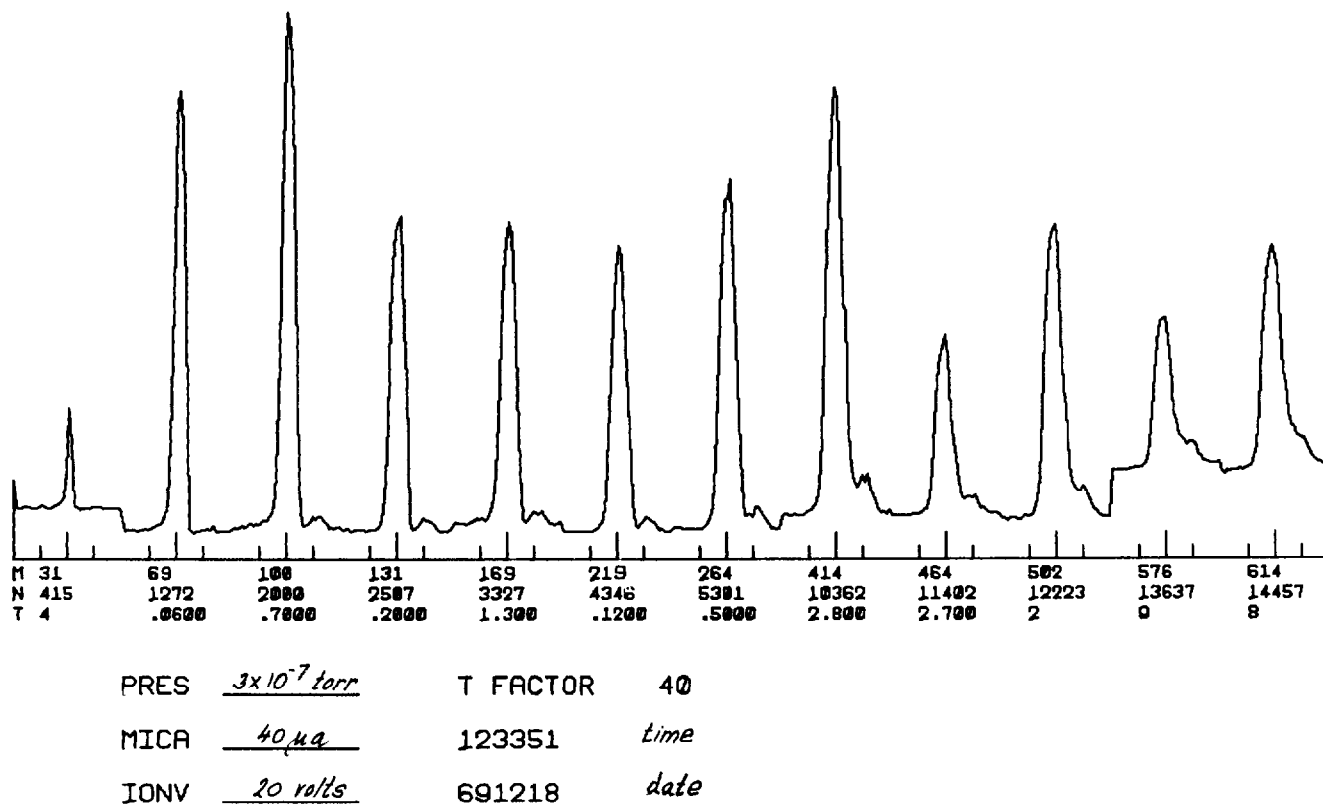
(18) W. J. Sanders, G. Breitbard, G. Wiederhold, *et al.*, "An Advanced Computer for Medical Research," *Fall Joint Computer Conf. Proc.*, ACM, Anaheim, Calif., 1967, p 497.

**Table I. A List of Program Options**

- (1) **CALIBRATE:** Creates an accurate  $N$  Table. The  $N$  numbers which correspond to the peaks in the reference gas are used as the end points of a piecewise linear interpolation procedure for calculating a complete  $N$  Table.
- (2) **COLLECT:** Is the primary data collection step. It is here that the 750  $N$  Table values are sent to the MS and the 750  $m/e$  intensities recorded. This operation can be repeated at five-second intervals as the data are filed on disk under an experiment name.
- (3) **TYPE:** Allows the user to print out spectral data by indicating what spectra in a given file are to be reviewed. The user can request that the amplitudes of particular  $m/e$  positions be typed; that a given number of the highest amplitudes be typed, or that a consecutive number of them over a given range be typed.
- (4) **PLOT:** Enables the user to have bar graphs produced by the computer controlled digital plotter. The amplitudes to be plotted can be selected with the same flexibility as described in TYPE.
- (5) **SUM:** Produces a plot of the total ion current over a series of gathered spectra. All responses of a spectrum are summed to produce one datum point on the plot. This plot corresponds closely with the GLC output when running with the GLC.
- (6) **TRACE:** Produces a record of a spectrum similar to the normal chart recording output. The analyzer is sampled at all  $N$  values (about 10 per amu) over a given range and the result is plotted as a "broken line." (Used for system check out)
- (7) **MONITOR:** Provides for inspecting the peak profiles by sampling the spectrum around a given  $m/e$  position. The gathered data are then typed out. (Normally used for system service or service log)
- (8) **DISPLAY:** Enables the user to display a given mass position (or  $N$  number) in the center of the console oscilloscope. (Used in the adjustment of the mass spectrometer)
- (9) **GAS:** Allows the user to remotely turn the reference gas on or off. This is helpful when operating the system from a remote position.

The example of a user-computer conversation given in Figure 2 represents the day-to-day computer-researcher dialogue given to direct the system's operation. Deeper level programming may be done at the terminal to redefine these functions or to add new modes. Additional system development may be done by the chemist-user, or his programmer in a manner typical of general purpose computer software. In normal daily practice, the user first requests the calibrate function and then proceeds to data acquisition, analysis, and presentation. Usually the calibration is done once every four hours.

It is this calibration subsection of the program that assigns to each integer mass position a value  $N$  which when sent to the D-to-A converter in the interface, will set the mass analyzer to pass that particular species of  $m/e$ . During this calibration phase a reference compound (perfluorotributylamine, FC-43), is introduced into the MS. The calibration procedure in addition to determining the  $N$  values, makes data available that will aid the operator in making qualitative judgments about the stability, sensitivity, and resolution of the MS. Also a service or maintenance record plot is available (see Figure 3), that, at least indirectly, shows these and other important instrument conditions. Figure 3 is actually 12 traced segments of a complete spectra, each segment covering a span of about 4 amu and each taken at a different integration time (gain). The  $m/e$  value, its position, and a parameter indicating the gain is automatically printed below each peak. The date and time is printed by the computer, but at present the operator must insert the sample pressure and ionization parameters. The file of these plots represents an excellent record of the instrument's serviceability. The calibration is automatic and its use less complicated than the description. It takes about 5 minutes, after which the reference gas is pumped out of the system. In the IBM 360-1800 system, the time is used to compile the main program.



**Figure 3. A monitor plot indication of instrument serviceability**

Total spectral data acquisition time depends upon the number of  $m/e$  positions measured and the integration time allowed per position. It may be calculated:

$$\text{Spectrum acquisition time} = P \times (T_i + T) \quad (1)$$

where  $P$  is the number of  $m/e$  positions to be measured (they do not have to be contiguous or sequential),  $T_i$  is a transition time (2 msec in our system), and  $T$  is the integration time per peak (nominally 6 to 17 msec, but we have usefully used 1 to 1000 msec).

Normally data are collected at each integer  $m/e$  position 1 through 750. The 750  $N$  values are sent through the D-to-A converter to the MS and the 750 responses (a full spectrum) are recorded by the computer via the A-to-D converter. This process can be repeated approximately every 5 to 10 seconds for an arbitrary number of times. The spectra thus gathered are stored by the computer on magnetic disks or tapes. Program changes may be made to measure any subset of the 750  $m/e$  positions and thus achieve faster repetitive spectra. Conversely more measurements may be made at any specific peak position, a technique which may be used for accurate isotopic ratio measurements.

Since many spectra are taken and stored during a GLC run or a solid probe experiment, the user requires fast methods to evaluate the data. The more useful data abstracting programs we use are:

**THE MATRIX SEARCH.** The user specifies which group of spectra, what range of mass values in each spectra, and how many large peaks he wants abstracted from each spectrum. An abstract of these highest peaks is then typed out and in many cases this abstract contains useful chemical information or at least indicates the spectrum of interest.

**THE TIME PRESENTATION (PLOT).** This is a computer drawn plot of certain peak intensities or a sum of all peak intensities of each spectrum (total ion current) plotted against time. The latter gives a good reproduction of the GLC curve and also indexes the spectra of interest (19).

**NORMALIZED SPECTRUM PLOTS.** Conventional bar graphs of mass *vs.* time, normalized and annotated, are routinely available.

All data outputs are in the laboratory and are available immediately after data acquisition. All spectra are filed and may be recalled at a later time or date and reprocessed in any way desired.

Involved programs of these magnitudes are specifically dependent upon the language of a given computer. The logic may be easily transferred, but in general the specific program may not. We have about 4 man-years of programming invested in this system.

## THEORY OF OPERATION

During spectrum data acquisition, the computer directs the mass analyzer to a program-selected mass position and reads the output intensity of the MS. The mass analyzer is not swept in a conventional sense. As indicated in Figure 1, it is controlled by a voltage ( $V_c$ ) such that

$$m/e = f(V_c) \quad (2)$$

where  $m/e$  is the mass/charge ratio and  $f(V_c)$  is a monotonic function characterized by the MS. For every  $M_i$ , ( $M = m/e$ ), to be passed by the mass analyzer, the computer has (according to the prior run calibration program) a digital number  $N_i$

which is transformed by the D-to-A converter to the voltage  $V_{ci}$ .

The determination of these values,  $N_i$ , is accomplished by the calibration program. The value of  $N$  for 12 key peaks of the reference compound are known to approximately 1 amu from prior calibrations. The actual  $N$  value for the centroid of each of these peaks is then determined by detailed examination of the  $m/e$  continuum in each of these areas. Sufficient detail is obtained by designing the D-to-A resolution to be 10 or more values per peak width.

After determining these exact 12  $N$  values, linear interpolation, superimposed upon the analytical function,  $m/e = f(V_c)$ , is used to expand the list of 12 experimentally determined values to a full table of 750 entries. (The analytical function of  $m/e$  to control voltage is linear for the quadrupole and parabolic,  $m/e = k(V_c^2)$ , in the case of the T-o-F MS.)

Thus the procedure to measure the intensity at any  $M_i$  is as follows: *a.* The number  $N_i$  which corresponds to the selected  $m/e$  ratio ( $M_i$ ) is loaded from the computer into the D-to-A converter. This sets the control voltage,  $V_c$ , to the mass analyzer. The output of the mass spectrometer is proportional to the quantity of ions,  $M_i$ , passed from the sample.

*b.* An analog circuit, reset and released by the computer, integrates the output of the MS.

*c.* Several milliseconds after the integrator is released, (the choice of integration time was initially supplied by the user upon program request), the computer samples the output of the integrator by means of an A-to-D converter. This digital value is stored as the intensity of  $M_i$ .

Steps (*a*) through (*c*) are repeated to acquire a complete spectrum.

The fundamental restraint upon this system is the drift of the function  $m = f(V_c)$  following calibration. Our experience with the Finnigan 1015 and a Bendix T-o-F instrument and our interface, is that this drift causes an error in  $N$  of less than  $1/8$  the value from one  $N$  entry to the next in a 1-hour period. This is sufficiently small to allow an unambiguous mass identification.

Table II contains comparisons of signal-to-noise ratios and the following defined figures of merit. The comparisons are made between the described control system, a linear scan in time, a parabolic scan in time such as the T-o-F, and the exponential time scan characteristic of magnetic instruments.

Uniform conditions are used to give realistic values for comparison; it is assumed that in each case the peak shapes are uniform if scanned in time, and that they are gaussian, and that the resolution is commensurate with the 10% valley (5% points on a single peak side) definition (3). In order to give typical comparison figures, it is further assumed that a spectrum will be taken from mass 50 to 500 in 4500 milliseconds.

The first column in Table II is the time the mass analyzer is on or about the mass position. In the case of the computer control system, the 4500 milliseconds is divided equally into 450 periods of 10 milliseconds each. Two milliseconds are allowed for each transition, and the mass analyzer will dwell on the peak position for 8 milliseconds. In the case of a conventional linear scan, the analyzer will enter a peak area and leave it 10 milliseconds later. By the 10% valley convention, this means the time from the beginning 5% level to the end 5% level of a single peak. However for the parabolic case (the T-o-F) it will be found that the resolution of the instrument will have to be set for the work case, peaks 499 and 500. It will be found that there is 6.6 milliseconds between these peak

(19) R. A. Hites and K. Biemann, "Advances in Mass Spectrometry IV," Elsevier Publishers, Amsterdam, 1968, p 37.

Table II. A Comparison of Attributes Affecting Signal-to-Noise Efficiencies

Typical Operation Condition: Scan from  $m/e$  50 to 500 in 4500 Milliseconds

Type of scan	Time on, or between 5% points, of a peak, msec	Time constant of amplifiers, msec	Ions detected: (Peak intensities of $n$ ions/msec)	Effective noise bandwidth, Hz	Figure of merit: $1000/n \times$ detected ions/bandwidth
Control and integrate	8	N/A	$8.0 n$	40	200
Linear scan $m = kt$	10	2	$5.1 n$	80	64
Parabolic scan $m = kt^2$	6.6	1.3	$3.4 n$	120	28
Exponential scan $m = m_0 e^{kt}$	3.9	0.8	$2.0 n$	200	10

centers, and the theoretical 5% heights must be at the midpoint. Since all peaks are similar, all peaks of the scan will be just 6.6 milliseconds from 5% point to 5% point. During 34% of the scan time, the analyzer is not in the area of any peak position at all; but is mostly between peaks in the low mass range. The case of the exponential scans is similar. In this case it will be found that the peaks are 3.9 milliseconds wide and 61% of the time no information can get through the instrument.

The next column indicates the time constant ( $\tau$ ) of the amplifier channel appropriate to the scan parameters. The control system uses a full integrator, so the entry is not applicable. In the conventional scanning system, the time constant is usually chosen as large as skewing permits to integrate signal and discriminate against noise. The relationship between  $\tau$  and the 3-db bandwidth ( $f_{bw}$ ) of an amplifier is simply  $\tau = 1/(2\pi f_{bw})$ . If  $\tau$  is chosen to be large, peak skewing and broadening as illustrated in Figure 4 will occur. If  $\tau$  is chosen small, the bandwidth with its attendant noise is excessive and there is little integration of the signal.

This is the dilemma always faced by the user of linear amplifier circuits: the desire to limit amplifier bandpass to smooth the signal, as opposed to the need for a wide bandpass to pass

the signal without distortion. Since the purpose here is to compare our described amplifier and integrator system with conventional linear amplifiers, a  $\tau$  of 0.2 is assumed for the conventional case. This  $\tau$  is still large enough to cause degradation of resolution in the conventional output signal (25 to 35% depending upon the definition used). It is felt that this choice represents a fairly typical operational parameter. The assumption of a rigorous lower value would result in an unnecessary, and perhaps unrealistic, comparison advantage for the described control and integrate signal system.

The column "Effective Noise Bandwidth" is the  $f_{bw}$  for the time dependent scans. However an equivalent 3-db bandwidth is not as well defined for the integrator. It can be shown that for an integration interval,  $T$ , (8 milliseconds in this example) an  $f_{eq}$  may be determined such that a linear amplifier of bandwidth  $f_{eq}$  would pass the same amount of "white" noise as the integrator. The actual bandpass of an integrator is a  $\sin(x)/x$  type function.

The white noise power passed by either system may be expressed as an integration of the white noise model,  $e^{j\omega t}$ , (20)

(20) W. B. Davenport, Jr., and W. L. Root, "Random Signals and Noise," McGraw-Hill, New York, 1958, p 88.

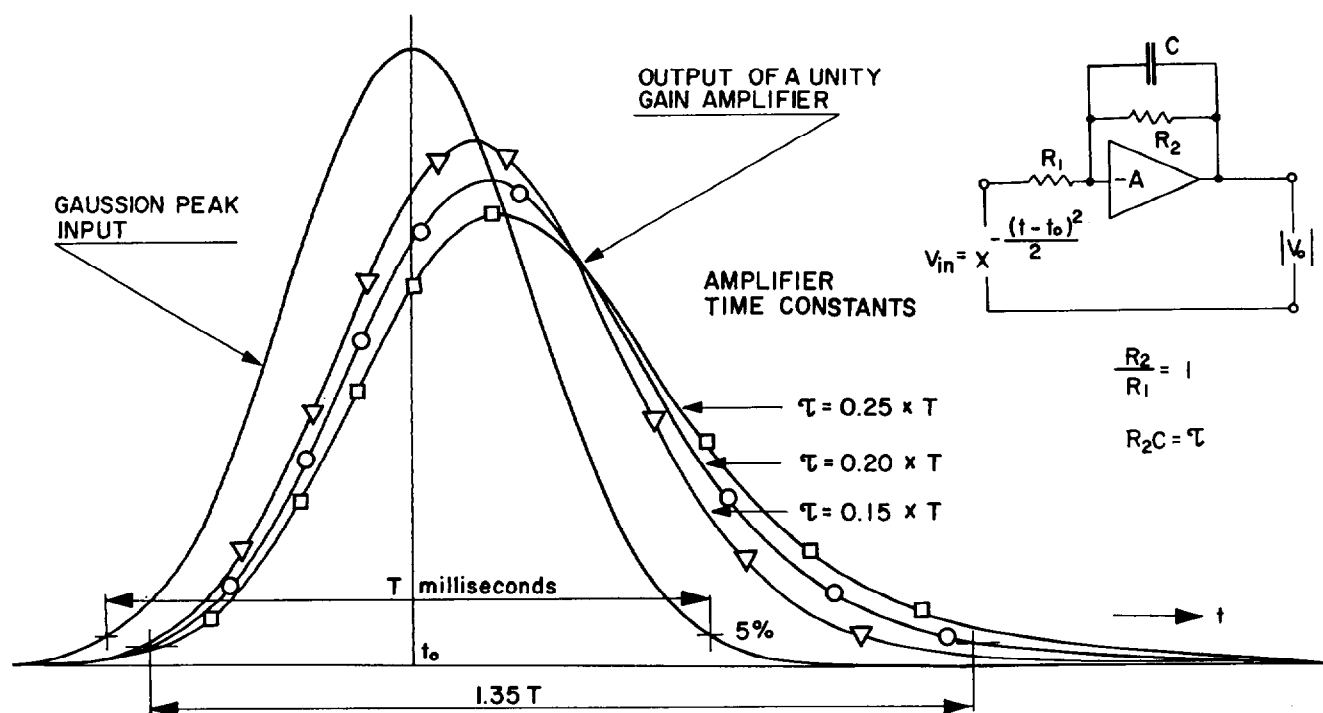
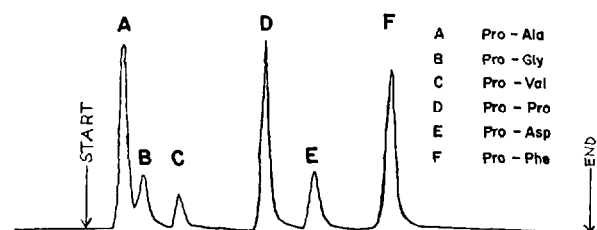
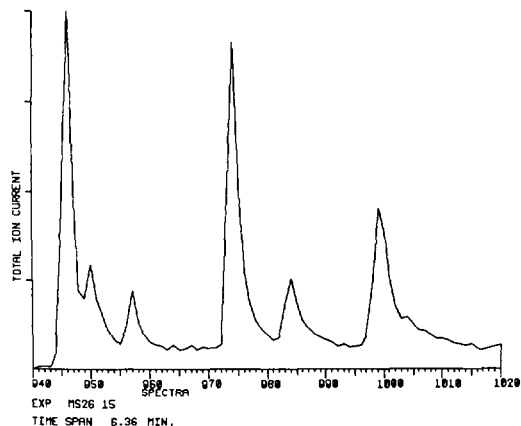


Figure 4. Peak broadening and skewing effect of narrow bandwidth amplifiers



GLC CHART RECORD OF TFA - DIPEPTIDE METHYL ESTERS



A COMPUTER PLOT OF THE SUMMED PEAKS (IONS) OF EACH SPECTRUM

Figure 5. The above trace is a GLC flame ionization chart of an experiment. Below is a total ion plot, created, and plotted by the computer, that indexes the individual spectra

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OPTION =?TYPE
EXPERIMENT# =?MS26_15
FROM SPECTRUM =?955
TO =?960
BY MASS, AMP, or ENTIRE =?AMP
FROM MASS =?30
TO =?750
NUMBER =?9
SPECTRUM 955
MASS 31 42 43 46 57 69 139 166 167
AMPL 103 22 22 26 22 30 23 37 27
SPECTRUM 956
MASS 31 45 46 69 70 96 139 166 167
AMPL 117 25 25 32 33 27 33 64 44
SPECTRUM 957
MASS 31 43 45 69 70 72 139 166 167
AMPL 124 38 39 57 44 52 47 102 76
SPECTRUM 958
MASS 31 43 45 69 70 72 139 166 167
AMPL 114 31 32 36 31 34 32 60 48
SPECTRUM 959
MASS 31 43 56 69 70 96 139 166 167
AMPL 116 26 24 26 27 25 29 51 39
SPECTRUM 960
MASS 31 32 45 46 69 70 72 166 167
AMPL 113 22 24 23 25 24 21 36 30

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Figure 6. The principal peak listing from the matrix search

times the circuit transfer function over the frequency range in  $\omega$ . The first shown below (on the left side of the equation) represents the white noise retained by a full integrator during a time interval  $T$ . The second expresses the white noise passed by a simple amplifier of bandpass,  $f_{eq} = 1/(2\pi\tau_{eq})$ .

$$\int_0^\infty \left| \int_0^T e^{j\omega t} dt \right|^2 d\omega = \int_0^\infty \left| e^{j\omega t} \frac{1}{1 + j\omega\tau_{eq}} \right|^2 d\omega \quad (3)$$

A solution for  $\tau_{eq}$  may be made by numerical methods:

$$\tau_{eq} \cong 0.496 T \quad (4)$$

Using this value, it is found in the example that  $f_{eq} = 40$  Hz.

A last analytical benefit of the system is the efficiency of detecting ions. In any MS with electronic ion detection, an ion is detected or not detected and there is no "5% detection."

There is a 5% probability an ion generated in the source will pass the analyzer and hit the detector. Or more accurately, if when a peak is "centered,"  $n$  ions register upon the detector each millisecond, it may be expected that at the appropriate low side of the peak,  $n/20$  ions will register each millisecond. The control method is always "centered" upon the peak, hence the total expected ions will be  $T \times n$  ions. However, in scanning a gaussian peak, it can be shown that for an equivalent time, from the first 5% point through the maximum and out to the last 5% point, the total expected ions will be approximately  $0.51 \times T \times n$ , where now  $T$  is the time from 5% point to 5% point. These numbers of ions expected to register upon the detector are tabulated as "Ions Detected" in Table II. Many small, but important, peaks will have an  $n$  of 1 to 10 ions per millisecond under the operating conditions imposed by some modern research requirements.

A figure of merit for comparing the systems may be defined:

$$\text{Figure of Merit} = \frac{1000}{n} \times \frac{\text{Detected Ions}}{\text{Bandwidth (Hz)}} \quad (5)$$

This is the final tabulation in Table II. Our use of the system has verified these results, that introducing computer control to the quadrupole or T-o-F MS can enhance the useful sensitivity by a factor of 3 to 8. The greater convenience offered to the user is not at the expense of performance, but offers these intrinsic advantages.

One other practical benefit is possible by reviewing the attributes of resolution. The idealized gaussian peak considered here, which has a width commensurate with the 10% valley resolution criteria, has a contribution of only 0.06% at the neighboring integer mass position. Since in the control method, only the cross contribution at the integer positions is harmful for some experiments, the resolution may be degraded until a 0.5% or 1% cross contribution is observed. If the physics of the particular instrument are exploited, it will be found that this will greatly increase the portion of generated ions that will be passed by the analyzer.

Some consideration should be given here to the software and its interaction with the user and the instrument. A mode of conversation has been programmed into the system to prompt the user for necessary parameters, and then expand upon these parameters to conduct the necessary detailed operation of the instrument. In retrospect we find that we have very closely followed the concept of R. J. Spinard (21). A similar problem occurs with the presentation of information, which is often too voluminous for complete display. To overcome this, the bulk of the information is held in the computer, and is made available by similar conversational techniques.

It should be realized that the present software is in an embryonic state of development compared to its eventual potential. The system of computer, interface, and MS may be defined in terms of computer syntax to a systems developer in a manner comparable to the definition of a specific data processing task to a system programmer. There is an enormous potential in the implemented syntax of this instrumentation system for the chemist who may have special requirements and who understands fully the principles of the augmented instrument. The user can then program, or have programmed, efficient solutions to many of his instrumentation problems.

The features that do allow the foregoing benefits, do themselves impose certain limitations. The control system does not normally return any information about doubly ionized odd

(21) R. J. Spinard, *Science*, **158**, 3797, 55 (1967).

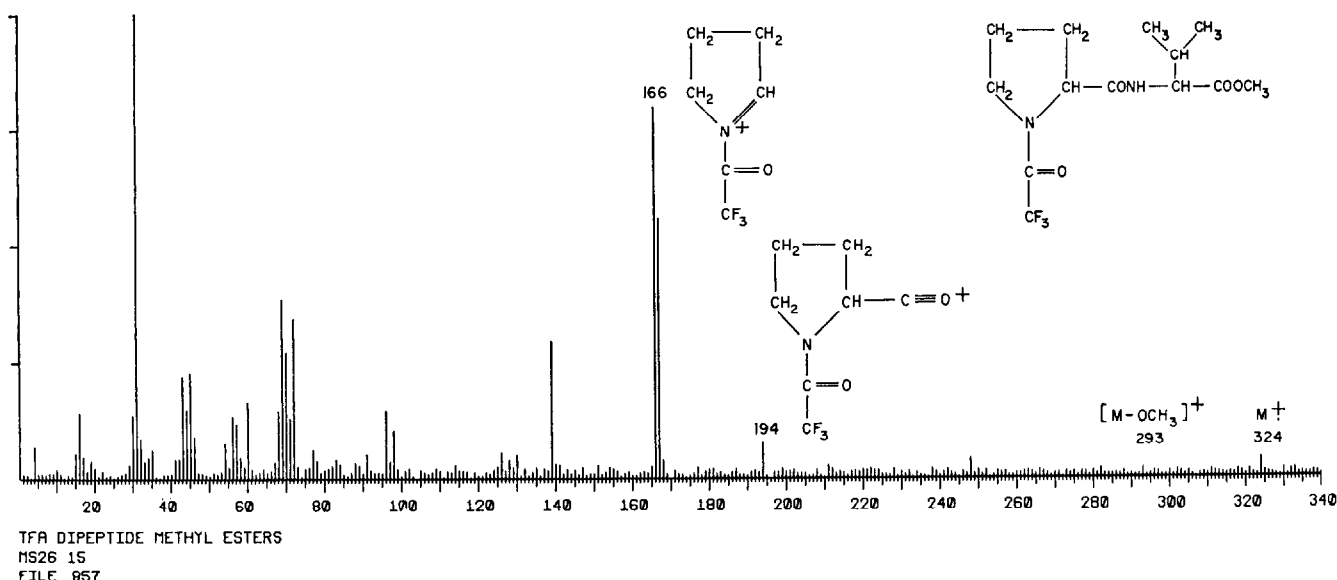


Figure 7. The on-line, computer plotted spectrum

mass values (peaks at 0.5 integer position), wide metastable peaks, or the value of mass defects. It also might be expected that mass defect deviations, especially at high  $m/e$  values, would cause difficulty. In practice there have not been any problems attributed to this latter case, the high  $m/e$  defect. The resolution and other operational factors have masked this inherent difficulty. If operational use should be hampered by this problem, we have proposed techniques of concurrent calibration on the unknown peaks themselves.

For example, the major peaks in the unknown compound, identified to their nominal integer value (less mass defects), would be used to calibrate the  $N$  table. After a programmed computer decision to explore a peak area, similar to those illustrated in Figure 3, the computer would direct the "scan" to that area. Data acquisition time would be about 100 msec for 10 data points over the peak profile. Centroid identification and recalibration might be another 100 msec. If this were repeated for 8 or 10 key peaks, total recalibration would be in the order of 2 sec. This technique could also be employed to verify the linearity above the last reference peak (614 with our system) or below the first. (We have paid little attention to  $m/e$  below 12 or 18.)

As a final minimal operating mode, the scan could be programmed to simulate any present mode of time-based scan and data collection, with comparable attributes of performance. As an example, doubly ionized masses or metastable peaks might be identified and measured. Of course the MS used must have sufficient resolution and/or sensitivity, also the total spectrum acquisition time would be increased. Such changes of operational mode would be by program only; hence they could be established or removed in milliseconds with no hardware or switch changes of any nature.

## RESULTS

In a typical experiment a mixture of TFA-dipeptide methyl esters (22) was injected into the GLC-MS system, and 130 complete mass spectra were collected and recorded by the computer. Eighty-one of the individual spectra were summed to obtain the total ion plot (Figure 5) (19). This may be compared with the GLC flame ionization chart record on the top. The mass spectral output from peak "C," for example, in the

(22) B. Halpern and J. W. Westley, *Biochem. Biophys. Res. Commun.*, **19**, 361 (1965).

region of scans 955 to 960, was then abstracted by the TYPE routine and the results are shown in Figure 6. This data shows that Peak C is homogeneous and that a satisfactory normalized plot can be obtained from scan No. 957. Figure 7 is the plot as produced in the laboratory. The background in the mass spectrum is primarily due to the GLC column bleed. Only the chemical notation was added by hand.

The taking of spectra, in this computer-compatible form, opens the way to many types of further processing: searching through each stored spectrum to pick out the amplitude at a specified mass position and plot this data to show the variation of the ion current of a specific  $m/e$  with time; check the homogeneity of each GLC peak; resolve the mass spectra of simple mixtures into those of the individual components; and subtract background signal from a mass spectrum.

The system is also well suited to the recording of spectra from solid samples introduced directly into the ion source. Because of the fast scanning speed and the recording of many spectra, there is no need to establish a constant vapor pressure in the mass spectrometer and any contamination or decomposition of the sample is readily detected.

## CONCLUSION

It is feasible to build a limited purpose computer and a quadrupole MS as one unit, forming a compact instrument with features similar to the system presented in this report. In addition, some of the software could be embodied in hardware circuits. Such units would be more costly than those using commercial general purpose computers, but could be uniquely well adapted to space or other special physical environments. Alternatively, the system can be interfaced with a larger time-shared computer.

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